Exposure & Health Risks of Domoic Acid in Marine Wildlife & Humans

Photo by Paul Nicklen

Wildlife Algal-toxin Research and Response Network for the U.S. West Coast (WARRN-West)

WARRN-West and Biomedical Diagnostics

Kathi Lefebvre, Program Leader
Anne Baxter, WARRN-West Manager

Funding & Research Support

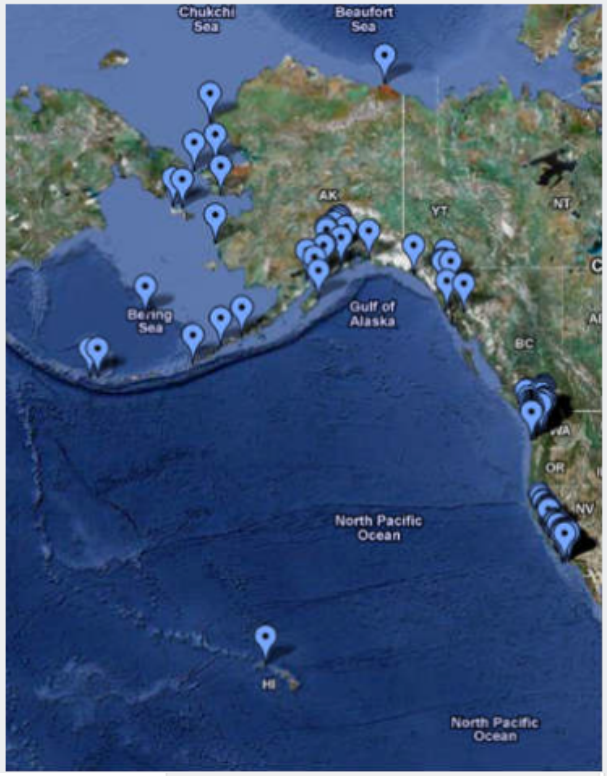
NOAA's Ocean and Human Health (OHH) Traineeship program
ECOHAB (Ecology and Oceanography of Harmful Algal Blooms) program
NOAA's Office of Protected Resources
NWFSC Research Plan Near Term Priority 5

What is WARRN-West?

Algal toxin exposure can impact the health of many marine mammals, including dolphins, whales, sea otters and sea lions. WARRN-West is a coast wide surveillance program that identifies algal toxin exposure in marine wildlife populations. We monitor for domoic acid (DA) (the toxin responsible for Amnesic Shellfish Poisoning) and for saxitoxin (the most potent toxin of the Paralytic Shellfish Toxins).

The sampling network consists of federal, state, public, private, and academic partners as well as the major marine mammal stranding networks on the US West Coast. All species of marine mammals are tested and results are available in near real-time.

In a complimentary study funded by ECOHAB, a biomedical model (zebrafish) is being used to find biomarkers indicative of chronic disease caused by DA exposure. This marriage of biomedical model and field exposed sentinel species will allow for development of effective biomarkers of disease that can be used to assess "at risk" human and wildlife populations



Related links

Marine Mammal Stranding Network Newsletter (Winter 2010)

http://www.nwfsc.noaa.gov/research/divisions/efs/warrnwest/

Prevalence of Algal Toxins in Alaskan Marine Mammals Foraging in a Changing Arctic and Subarctic Environment

Harmful Algae 55 (2016)

Kathi A. Lefebvre[1*], Lori Quakenbush[2], Elizabeth Frame[1,3], Kathy Burek Huntington[4], Gay Sheffield[5], Raphaela Stimmelmayr[6], Anna Bryan[2], Preston Kendrick[1], Heather Ziel[7], Tracey Goldstein[8], Jonathan A. Snyder[9], Tom Gelatt[7], Frances Gulland[10], Bobette Dickerson[7], Verena Gill[9,11]

- Northwest Fisheries Science Center
- Alaska Department of Fish and Game, Arctic Marine Mammal Program
- Alaska Veterinary Pathology Services (AVPS)
- University of Alaska Fairbanks, Alaska Sea Grant, Marine Advisory Program
- North Slope Borough Department of Wildlife Management
- Marine Mammal Laboratory, Alaska Fisheries Science Center, NOAA
- One Health Institute, School of Veterinary Medicine, University of California, Davis
- U.S. Fish and Wildlife Service, Marine Mammals Management
- The Marine Mammal Center
- Alaska Native Organizations: Western & Northern Coastal communities, Alaska Eskimo Whaling Commission, Native Villages of Gambell & Savoonga, Tribal government of St. Paul Island, whaling captains and subsistence hunters of Barrow.

Summary of Opportunistic Samples (n = 905)

- 905 marine mammals were collected between 2004-2013 and tested for the presence of algal toxins.
- Algal toxins were present in Alaskan marine mammals from SE Alaska to the Arctic Ocean.
- The data reveal that AK food webs contain algal toxins at levels that are detectable in top predators.
- **Most levels were low and health impacts were not confirmed.**

Species	Collection status	Collection period	Collection locations in Alaska (AK)	Total number of animals
Humpback	Stranded	July 2007 to Sept. 2011	Kodiak, The AK Peninsula, Southeast	8
Bowhead	Harvested	Spring & Fall 2006 to 2011	Barrow	25
Beluga	Stranded & Harvested	Sept. 2005 to Oct. 2012	Cook Inlet, Hooper Bay	15
Harbor Porpoise	Stranded	Aug. 2008 to July 2011	Cook Inlet	5
Northern Fur Seal	Harvested & Live Capture	2010	Saint George & Saint Paul Islands	179
Steller Sea Lion	Stranded	May 2004 to March 2013	Gulf of AK	42
Harbor Seal	Stranded	May 2008 to Aug. 2012	Gulf of AK, Egegik	9
Ringed Seal	Harvested	Nov. 2006 to Nov. 2012	Barrow, Chukchi Sea, Bering Sea	113
Bearded Seal	Harvested	Oct. 2007 to June 2013	Barrow, Chukchi Sea, Bering Sea	55
Spotted Seal	Harvested & Snow Urine	Nov. 2006 to Nov. 11	Barrow, Chukchi Sea, Bering Sea	158
Ribbon Seal	Harvested & Snow Urine	May 2009 to Oct. 2012	Barrow, Chukchi Sea, Bering Sea, Yakutat	21
Pacific Walrus	Harvested	May & June in 2012 & 2013	Saint Lawrence Island	82
Northern Sea Otter	Stranded & Live Capture	April 2004 to May 2011	Gulf of AK	193

SEAFOOD
Regulatory limit =
20 ug DA/g or
20,000 ng/g

Table 1: Summary of the number of domoic acid-positive individuals from 13 species of Alaskan marine mammals, including the sample matrix with the highest concentration. F = Feces, SC = Stomach Contents, S = Serum, IC = Intestinal Contents, U = Urine.

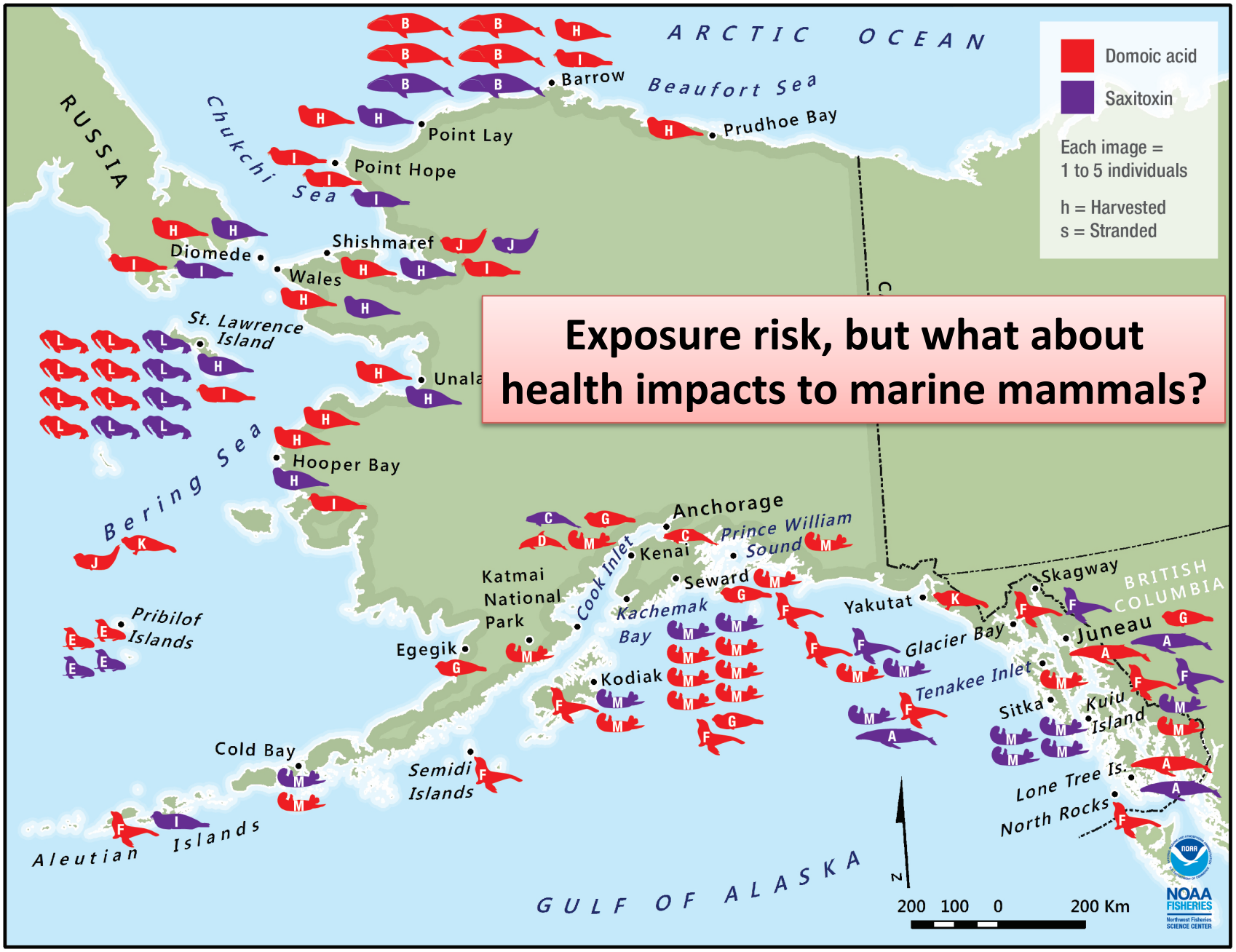
Species	Sample number	Number positive	% positive	Max conc. (ng/g or ml)	Sample Matrix
Cetaceans					
Humpback whale	8	3	38%	51	F
Bowhead whale	25	17	68%	359	F
Beluga whale	15	2	13%	7	SC
Harbor porpoise	5	2	40%	15	F
Otariids					
Northern fur seal	179	8	5%	13.8	S
Steller sea lion	44	12	27%	7	SC
Phocids					
Harbor seal	9	6	67%	8	F
Ringed seal	113	19	17%	127	F
Bearded seal	55	14	25%	48	IC
Spotted seal	158	5	3%	40	SC
Ribbon seal	21	5	24%	7	F
Odobenids					
Pacific walrus	82	34	41%	6,457	SC
Mustelids					
Northern sea otter	172	43	25%	162	U

SEAFOOD
Regulatory limit = 80 ug STX/ 100 g or **800 ng/g**

Table 2: Summary of the number of saxitoxin-positive individuals from 13 species of Alaskan marine mammals, including the sample matrix with the highest concentration. F = Feces, SC = Stomach Contents, IC = Intestinal Contents, U = Urine; na = not applicable.

Species	Sample number	Number positive	% positive	Max conc. (ng/g or ml)	Sample Matrix
Cetaceans					
Humpback whale	8	4	50%	62	F
Bowhead whale	25	8	32%	63	F
Beluga whale	12	1	8%	4	F
Harbor porpoise	5	0	0%	na	na
Otariids					
Northern fur seal	179	8	5%	42	F
Steller sea lion	42	4	10%	7	F
Phocids					
Harbor seal	8	0	0%	na	na
Ringed seal	110	15	14%	172	F
Bearded seal	44	6	14%	15	IC
Spotted seal	145	1	1%	3	SC
Ribbon seal	7	0	0%	na	na
Odobenids					
Pacific walrus	82	23	28%	240	IC
Mustelids					
Northern sea otter	163	37	23%	45	U


ARCTIC OCEAN
Beaufort Sea
Chukchi Sea
Bering Sea
GULF OF ALASKA
RUSSIA
ALASKA
U.S.A.
CANADA
YUKON TERRITORY
BRITISH COLUMBIA
Barrow
Point Lay
Point Hope
Prudhoe Bay
Diomede
Wales
Shishmaref
St. Lawrence Island
Unalakleet
Hooper Bay
Pribilof Islands
Aleutian Islands
Cold Bay
Semidi Islands
Egegik
Katmai National Park
Kodiak
Cook Inlet
Kachemak Bay
Anchorage
Kenai
Seward
Prince William Sound
Yakutat
Glacier Bay
Tenakee Inlet
Skagway
Juneau
Sitka
Kuiu Island
Lone Tree Is.
North Rocks
Domoic acid
Saxitoxin
Each image = 1 to 5 individuals
h = Harvested
s = Stranded
200 100 0 200 Km
N
NOAA FISHERIES
Northwest Fisheries SCIENCE CENTER
A Humpback whales (s)
B Bowhead whales (h)
C Beluga whales (s)
D Harbor porpoises (s)
E Northern fur seals (s)
F Steller sea lions (s)
G Harbor seals (s)
H Ringed seals (h)
I Bearded seals (h)
J Spotted seals (h)
K Ribbon seals (h)
L Pacific walruses (h)
M Northern sea otters (s)

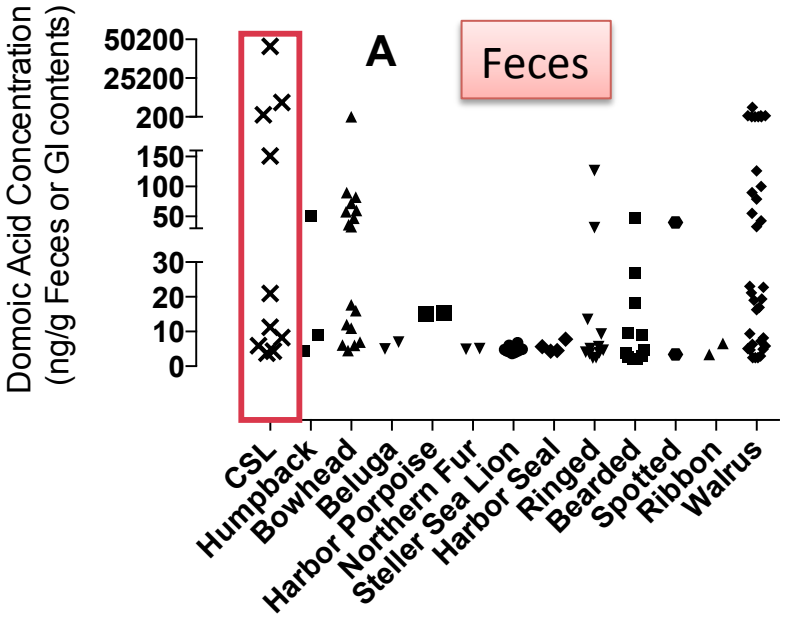


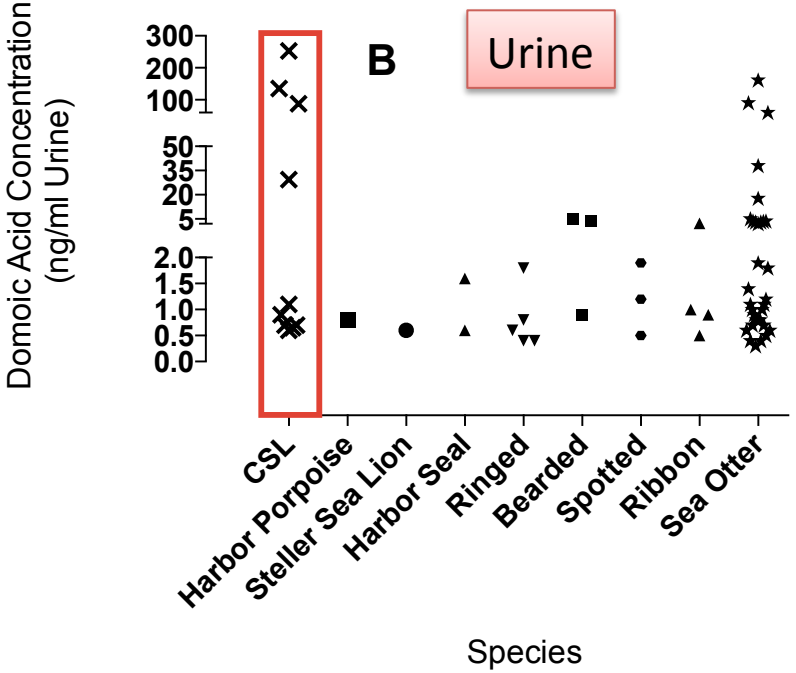
Exposure risk, but what about health impacts to marine mammals?

A Humpback whales (s)
B Bowhead whales (h)
C Beluga whales (s)
D Harbor porpoises (s)
E Northern fur seals (s)
F Steller sea lions (s)
G Harbor seals (s)
H Ringed seals (h)
I Bearded seals (h)
J Spotted seals (h)
K Ribbon seals (h)
L Pacific walruses (h)
M Northern sea otters (s)

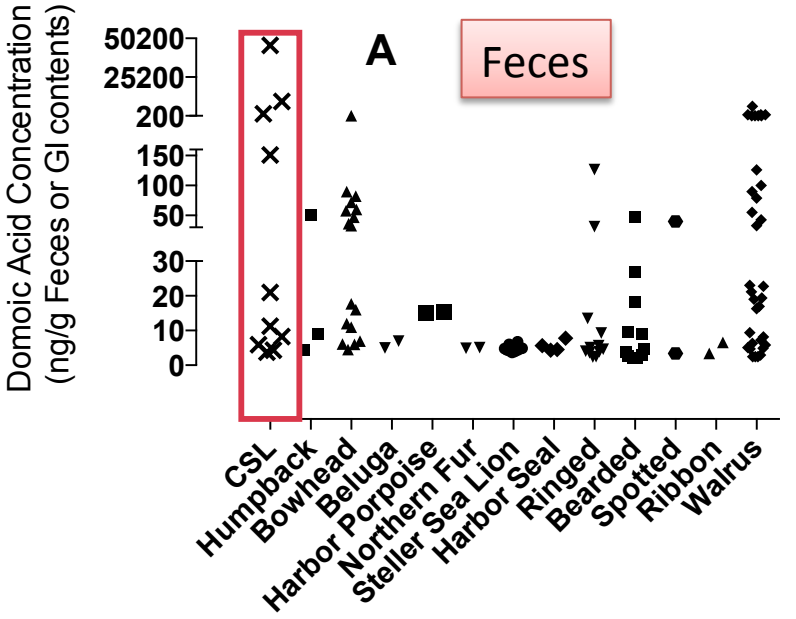
Classic Domoic Acid Toxicosis

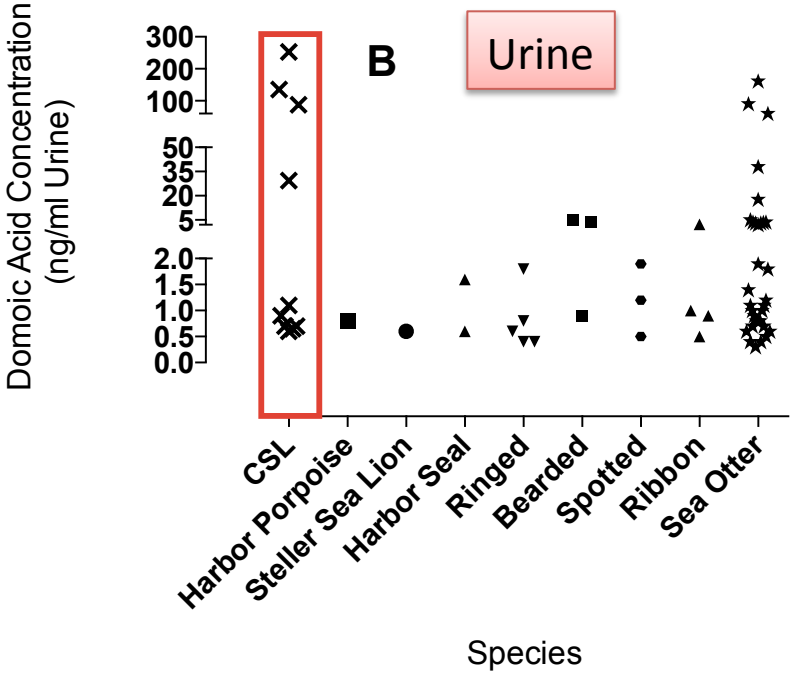
Feces range: **4 to 182,000 ng DA/ g**
Urine range: **0.6 to 253 ng DA/ ml**





Classic Domoic Acid Toxicosis





Feces range: **4 to 182,000 ng DA/ g**
Urine range: **0.6 to 253 ng DA/ ml**

Potential Lower limits:

- **200 ng/g** for feces?
- **50 ng/ml** for urine?
- **20 ng/g** for eye?

Algal toxin impairs sea lion memory & hippocampal connectivity, with implications for strandings

Peter F. Cook[1,2,*], Colleen Reichmuth[2], Andrew A. Rouse[2], Laura A. Libby[3], Sophie E. Dennison[4], Owen T. Carmichael[5], Kris T. Kruse-Elliott[4], Josh Bloom[4], Baljeet Singh[3], Vanessa A. Fravel[6], Lorraine Barbosa[6], Jim J. Stuppino[4], William G. Van Bonn[7], Frances M. D. Gulland[6], Charan Ranganath[3]

Peter Cook & Ronan

Effects of Chronic Low Level Exposure to Domoic Acid (NIH/NSF RO1)

University of Washington

Dave Marcinek

Preston Kendrick

University of California, Santa Cruz

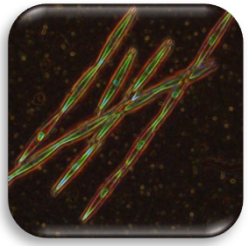
Don Smith

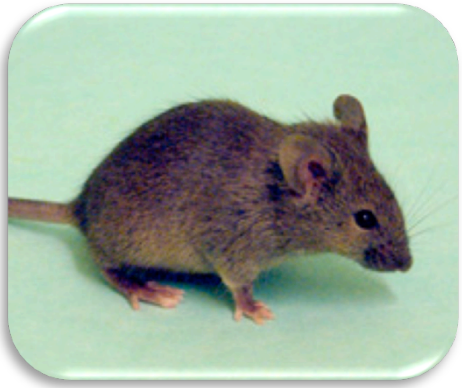
Yi Zuo

Emma Hiolski

Bridget Ferriss

Regulatory Limit = 20 ppm

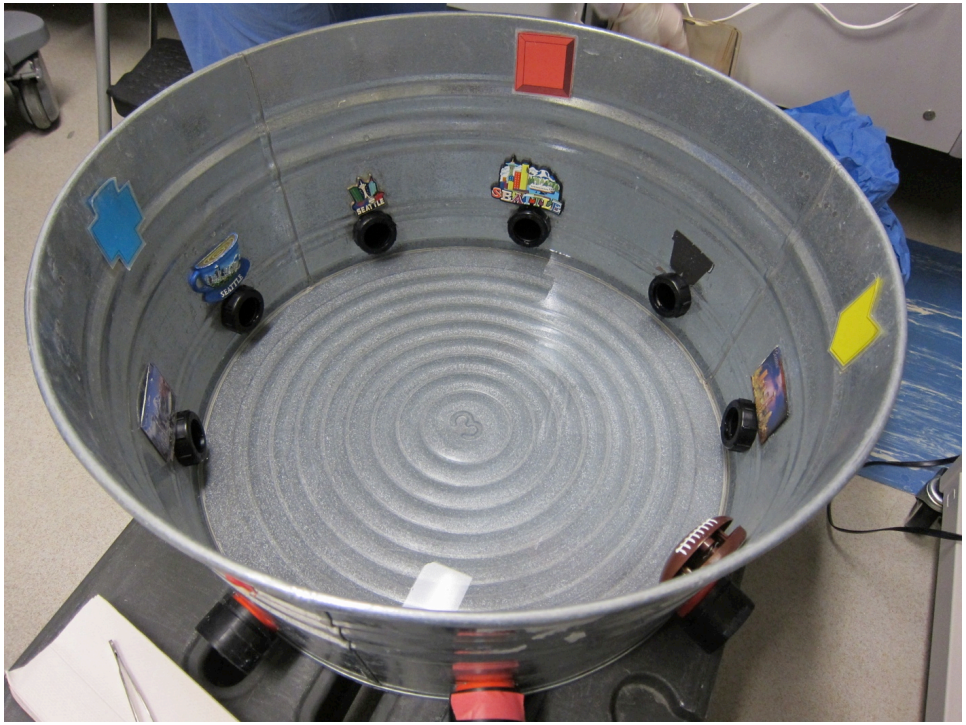




Mice were IP injected 1 X per week with 0.6 ppm domoic acid for 25 weeks (dose is 30% of EC50).

Radial Water Maze Testing Apparatus

After 6 months of exposure, mice were tested for learning & memory via a Radial Water Maze test (n = 20 control & 20 exposed mice).



Radial Water Maze Testing Apparatus

Radial Maze Test Results: CONTROL MICE

TRAINING DAY 1			TRAINING DAY 2			TRAINING DAY 3			TRAINING DAY 4			TEST DAY 5			TEST DAY 12		
RIAL 1	TRIAL 2	TRIAL 3	TRIAL 1	TRIAL 2	TRIAL 3	TRIAL 1	TRIAL 2	TRIAL 3	TRIAL 1	TRIAL 2	TRIAL 3	TEST 1	TEST 2	TEST 3	TEST 1	TEST 2	TES 3
177	180	180	79	40	180	90	103	180	4	77	180	180	177	87	180	180	180
180	180	180	122	180	96	140	2	180	180	90	153	108	66	180	180	180	180
180	26	34	58	3	25	16	167	5	11	28	2	8	4	6	8	14	2
51	180	180	107	41	93	180	125	3	27	33	27	31	2	56	91	12	29
180	123	15	180	86	178	179	24	41	69	48	35	39	32	3	62	37	12
180	180	139	180	10	51	71	95	123	55	31	164	105	13	9	180	65	10
180	97	31	56	83	5	64	103	72	180	75	37	178	52	3	180	180	180
180	180	5	33	34	72	142	180	143	104	5	6	101	5	3	104	3	92
180	29	67	77	180	7	180	56	100	54	3	6	42	5	3	9	39	28
68	180	17	180	72	20	95	4	38	28	4	5	5	15	109	69	5	13
180	170	16	180	139	38	128	99	180	130	122	180	180	180	155	180	180	6
180	50	22	145	157	61	180	156	104	180	180	128	125	63	34	4	3	2
180	133	40	180	119	149	180	180	163	84	64	180	180	17	24	1	16	68
180	165	22	180	180	180	113	180	3	10	59	180	22	66	55	25	9	25
39	44	180	180	147	148	17	4	4	93	179	7	26	41	17	36	23	61
180	63	22	45	65	53	180	180	43	180	44	180	108	2	180	180	180	180
135	136	58	170	124	66	165	123	3	65	13	19	42	35	6	14	9	9
180	25	160	65	97	47	155	180	9	7	57	4	2	24	24	55	36	180
166	98	180	180	175	31	28	105	12	2	5	9	1	15	7	3	18	7
180	175	56	67	31	14	39	10	11	23	15	10	58	8	18	12	9	2

CONTROL TREATMENT (6 months)

Radial Maze Test Results:
EXPOSED MICE

TRAINING DAY 1			TRAINING DAY 2			TRAINING DAY 3			TRAINING DAY 4			TEST DAY 5			TEST DAY 12		
TRIAL 1	TRIAL 2	TRIAL 3	TRIAL 1	TRIAL 2	TRIAL 3	TRIAL 1	TRIAL 2	TRIAL 3	TRIAL 1	TRIAL 2	TRIAL 3	TEST 1	TEST 2	TEST 3	TEST 1	TEST 2	TEST 3
60	180	14	180	14	180	180	180	180	180	180	180	180	180	180	180	180	153
63	41	53	9	23	180	180	180	180	19	180	180	180	180	180	180	180	127
180	180	180	180	180	180	180	82	77	180	162	180	180	180	180	180	180	180
161	29	180	180	43	121	36	130	102	180	180	180	180	180	180	180	49	19
62	180	180	180	180	180	8	117	14	180	180	180	180	180	180	180	180	180
180	16	50	13	37	180	180	180	180	114	180	143	149	180	180	18	21	8
180	180	180	180	180	180	180	180	180	180	180	180	180	180	180	180	180	180
76	180	180	65	180	180	113	102	72	180	180	45	180	102	171	74	26	16
180	180	180	180	180	180	180	180	180	180	180	180	180	180	180	75	153	36
180	180	180	180	180	180	180	180	180	180	180	180	180	180	180	180	180	69
180	180	180	180	180	180	180	180	152	180	180	180	180	180	180	180	180	180
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33	180	180	180	180	180	180	180	59	180	180	180	180	180	180	180	180	180
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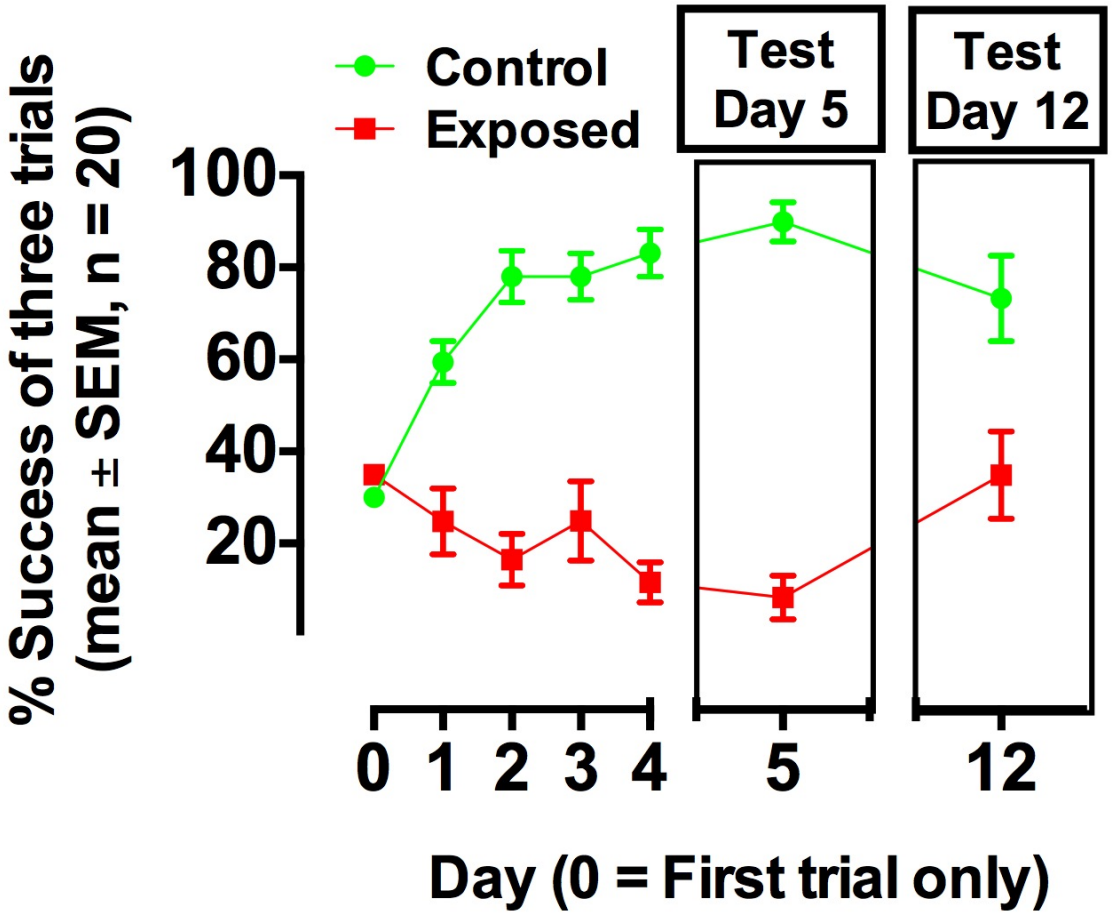
180	180	180	180	180	180	180	180	180	180	180	180	180	180	180	180	180	180
180	180	180	180	180	180	180	180	180	180	180	180	180	180	180	180	180	180

CHRONIC EXPOSURE TREATMENT (6 months)

Control

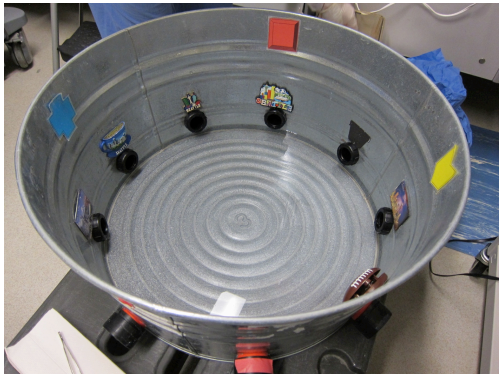
Exposed

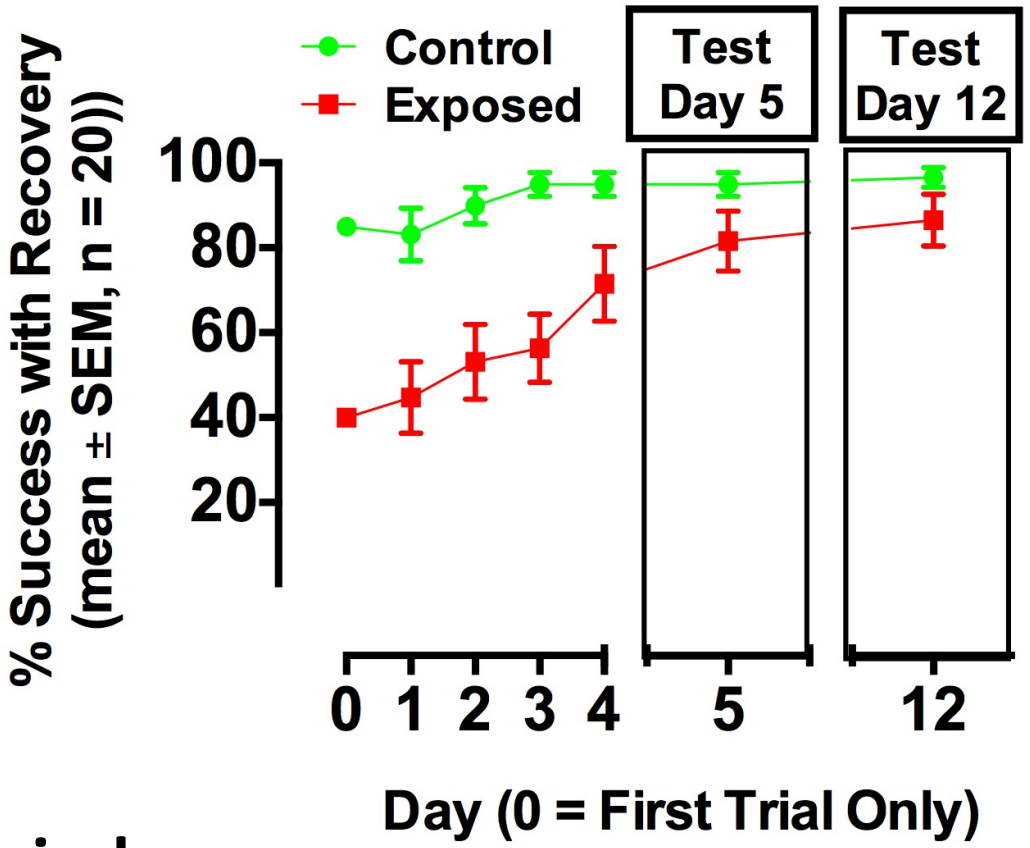
Significant Learning Deficits in Exposed Mice!



6 months of exposure

Learning Improved after 9 wk Recovery Period!

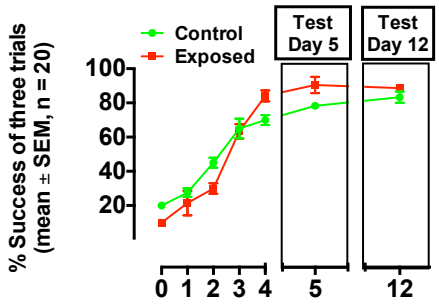




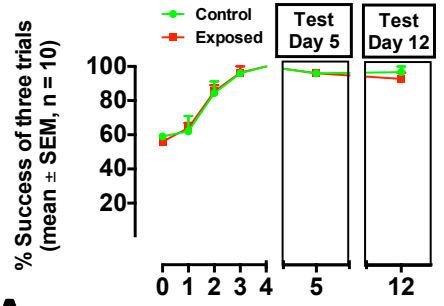
9 week recovery period

Does chronic exposure early in life impact cognitive decline with age?

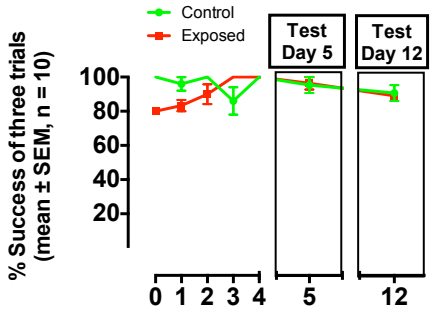
- Exposed once a week for ≈ 9 months
  - 3 to 12 months of age
- Tested at three old age time points;
  - 18 months (Early old age)
  - 24 months (Mid old age)
  - 28 months (Old old age)
- No exposure for 6, 12, and 16 months



Early Old Age

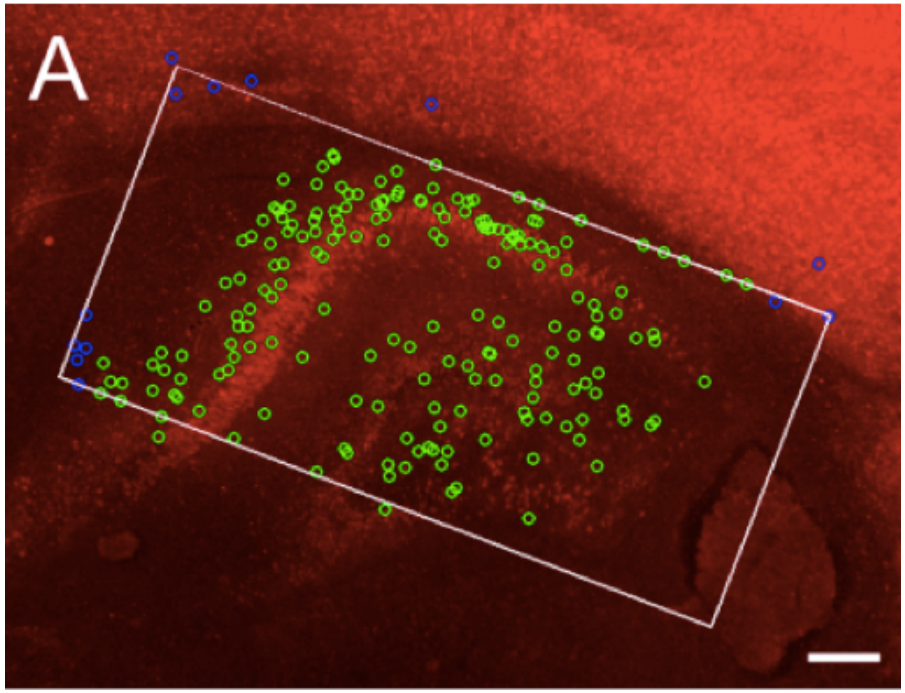


Mid Old Age



Old Old Age

Organotypic Brain Slice Cultures Mouse

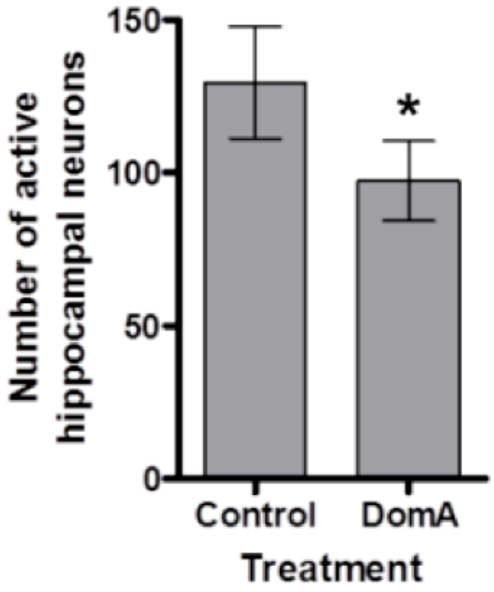


Emma Hiolski

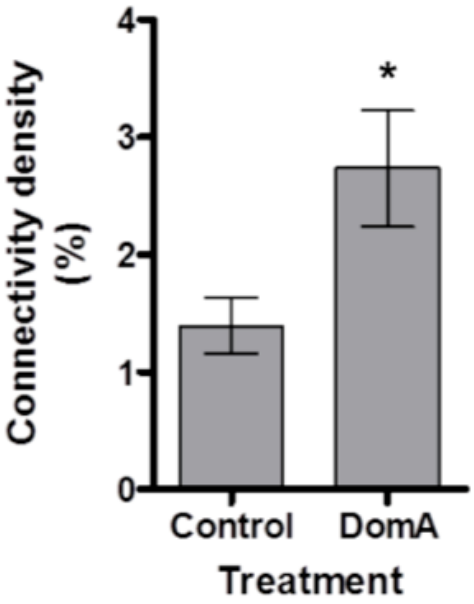
(A) Photomicrograph (x4 magnification; scale bar = 200 μm) of a representative brain slice culture (red staining = $NeuN^+$ neurons). White box highlights the region covered by the 512-electrode array, and electrophysiologically identified neurons (circles) are overlaid. Green circles = hippocampal neurons; blue circles = cortical neurons (excluded from analyses). (B) Mean (± SE) number of active hippocampal neurons in control (n=14) and domoic acid-exposed (n=15) brain slice cultures. * $p < 0.05$ (random effects ANOVA).

Electrophysiological effects of domoic acid exposure on the neural networks of organotypic brain slice cultures

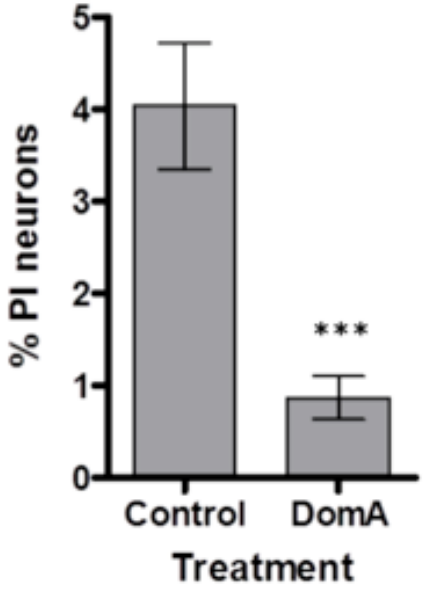
of Active Neurons



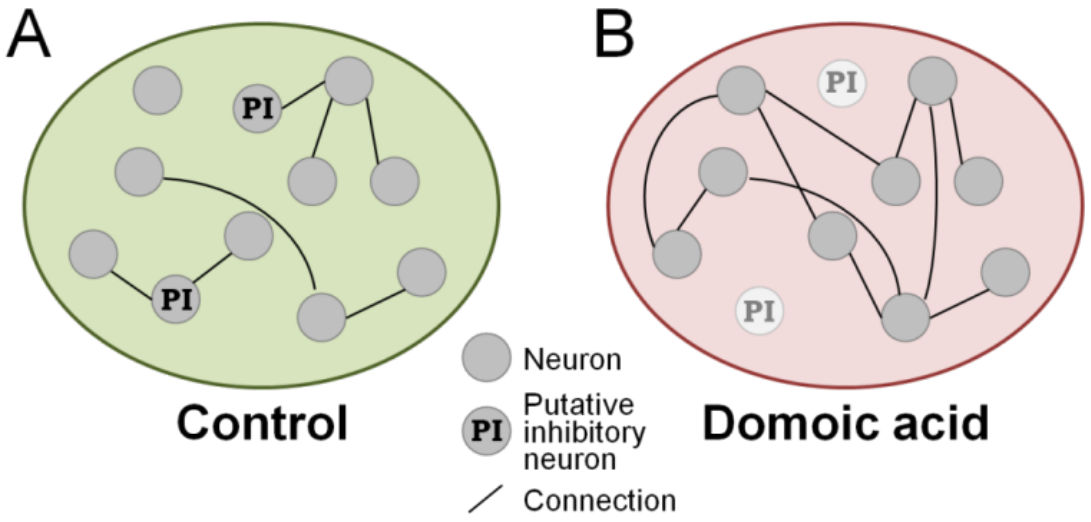
Connectivity Density



Percent Inhibitory Neurons



Model of domoic acid-induced changes in organotypic brain slice cultures



- Loss of inhibitory neurons with chronic exposure
- Increased connectivity & excitatory environment

Health Impacts of Domoic Acid

- **High exposures:** seizures, death, spatial memory/ learning deficits (permanent)
- **Low exposures:** Spatial memory/learning deficits, hyperactivity (reversible)

- **Potential consequences:**
  - Decreased navigational skills, stranding impacts?
  - Increased vulnerability to ship strikes, hunters, predation?
  - Compromised foraging ability, starvation?
  - Compromised immune function, vulnerability to infectious disease?

Ecological Forecasting for Domoic Acid Exposure Risks & Health Impacts in Arctic Bowhead Whale Populations

BIOLOGICAL

1. Fish biomass & recruitment	Bering Climate: http://www.beringclimate.noaa.gov/
2. Zooplankton species & density	Bering Climate: http://www.beringclimate.noaa.gov/
3. Primary production	Satellite record (MODIS/SeaWiFS)

PHYSICAL

1. Ice cover & retreat	NASA Distributed Active Archive Center (DAAC) at NSIDC
2. Temperature	NOAA/OAR/ESRL PSD, Boulder, Colorado http://www.esrl.noaa.gov/); Comprehensive Ocean Atmosphere Data Set
3. Mackenzie River discharge	Environment Canada
4. Wind speed, direction, mixing	Arctic Ocean Observing system (Wind)

CLIMATE

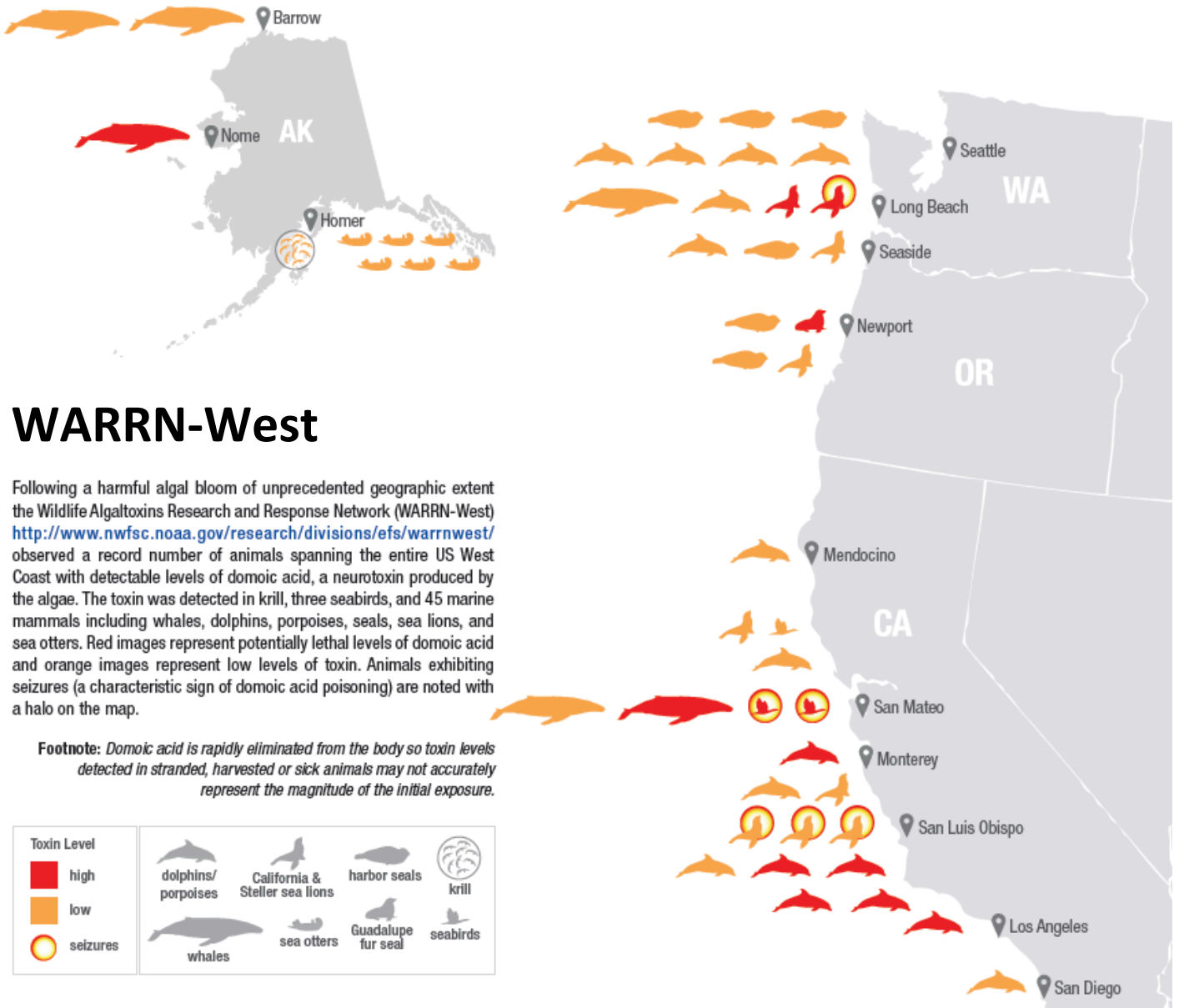
1. Pacific Decadal Oscillation (PDO)	NOAA Earth System Research Lab
2. Arctic Oscillation (AO)	NOAA Earth System Research Lab
3. North Pacific Gyre Oscillation (NPGO)	NOAA Earth System Research Lab
4. Northern Oscillation Index (NOI)	NOAA Earth System Research Lab

Bridget Ferriss

Proposal under review for North Pacific Research Board (NPRB) funding.

Domoic acid detected in marine wildlife from Northern Alaska to Southern California during a record-setting bloom of toxic algae in the North Pacific in the summer of 2015

NOAA FISHERIES
Northwest Fisheries SCIENCE CENTER



WARRN-West

Following a harmful algal bloom of unprecedented geographic extent the Wildlife Algaltoxins Research and Response Network (WARRN-West) http://www.nwfsc.noaa.gov/research/divisions/efs/warrnwest/ observed a record number of animals spanning the entire US West Coast with detectable levels of domoic acid, a neurotoxin produced by the algae. The toxin was detected in krill, three seabirds, and 45 marine mammals including whales, dolphins, porpoises, seals, sea lions, and sea otters. Red images represent potentially lethal levels of domoic acid and orange images represent low levels of toxin. Animals exhibiting seizures (a characteristic sign of domoic acid poisoning) are noted with a halo on the map.

Footnote: *Domoic acid is rapidly eliminated from the body so toxin levels detected in stranded, harvested or sick animals may not accurately represent the magnitude of the initial exposure.*

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WARRN-West Partners

- NOAA Northwest and Southwest Fisheries Science Centers,
- Alaska SeaLife Center,
- Cascadia Research Collective,
- Marine Mammal Institute Oregon State University,
- Portland State University,
- University of Washington,
- University of Alaska Fairbanks,
- University of California Davis One Health Institute.

ALASKA NATIVE COMMUNITIES

- NOAA West Coast & Alaska Marine Mammal Stranding Networks & Office of Protected Resources,
- North Slope Borough Department of Wildlife,
- Alaska Department of Fish and Game,
- The Marine Mammal Center,
- Washington State Department of Fish and Wildlife,
- Alaska SeaGrant,
- The Whale Museum of Friday Harbor,
- USGS National Wildlife Health Center,
- Alaska US Fish and Wildlife Service,
- Alaska Veterinary Pathology Service.